Non Invasive Blood Glucose Measurement

(Approved by RRC Members)

Synopsis of the PhD Thesis

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Abstract

Non-invasive blood glucose measurement using antennas is an emerging field of research that aims to develop a convenient and accurate method for monitoring blood glucose levels without the need for traditional finger-prick testing. This approach leverages the principles of electromagnetic waves and their interaction with biological tissues to estimate glucose levels. The procedure involves placing an antenna on the Human arm and monitoring variations in the resonant frequency, which is linked to changes in the blood glucose level. This is because the resonance frequency of the antenna is affected by the permittivity of the blood, which is dependent on glucose levels glucose estimate was modelled considering the antenna's frequency shifts in order to correlate the resonant frequency shift with the change in blood glucose in real-time. The designed antennas could successfully track the rise and fall of blood glucose using the glucose estimation model different levels of blood glucose. In this work, a non-invasive blood glucose measurement technique using Microwave Antenna Sensor is implemented. Today most of the wearable devices include antennas and relevant processing circuitry capable of non-invasive measurements. Various methods in the published literature for non-invasive blood glucose measurement where compared. A narrowband antenna is mounted on a human wrist for this purpose. After comparing different human body models it has been observed that all these models are di-electric tissue based models and do not have any provision to change blood glucose concentration.

Hence, a human body model for non-invasive blood glucose measurement is derived and implemented in this work. Uniqueness of proposed model lies in its ability to imitate the blood flow in the human body and ability to change the blood glucose concentration. The suggested model was evaluated to a standard dataset, and its accuracy was defined. It has been demonstrated through simulation that variations in blood glucose concentration also affect blood's electrical characteris-

tics, including electrical conductivity, dielectric constant, and other electrical factors. It was found that the range of blood glucose variation between 170 mg/dL and 450 mg/dL is between 1 and 3 dB values, whereas the range at the higher values of the glucose concentration has return loss variation in the range of 4 to 6 dB.

As next phase of the work, an electrically compact wearable adjustable antenna is designed to fit in onto a smartwatch dial. Proposed antenna has been tuned to human body parameters and resonates at 2.4 GHz band. A shorting pin was added to the antenna design, which was originally a basic monopole, to improve the return loss. Antenna PCB is fabricated using FR4 substrate with dielectric value 4.4 and height of 1.6 mm and radius of 17.5 mm. Return loss at 2.4 GHz is -24 dB and VSWR observed is 1.2 with the gain of 0.5 dB. Simulated and measured results of antenna are found in agreement.

In the final phase of the work, to validate the proposed design principle, the system working with a vector network analyser and a directional coupler has been have verified. The accuracy has been calculated using standard tool Clarke Grid Model and the final designed system was found to be 95% accurate. A mathematical correction factor is proposed which justifies the difference between finger pricking values, path lab results & actual experimental setup results.

Chapter 1

Introduction

1.1 Prevalence of Diabetes and Motivation

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Hyperglycaemia, or raised glucose levels, is a common effect of uncontrolled diabetes and over time results in serious damage to several of the body's systems [1]. In 2019, it has been reported that 463 million people worldwide have diabetes The number is projected to reach 578 million by 2030 and 700 million by 2045 due to changes in lifestyle and unhealthy diets [2-4]. Continuous glucose monitoring is crucial for glucose management and beneficial for hypoglycemia warnings, but it is invasive and inconvenient. A finger prick is required for each observation to collect and analyse a drop of blood for a normal blood glucose measurement.

Alternatively, non-invasive (without penetrating the skin) continuous glucose monitoring (CGM) has attracted extensive research leveraging techniques. However, most CGM devices are expensive, cumbersome to wear for an extended time, and sophisticated in terms of operation/maintenance, making them unattractive for both diabetic patients. The main aim at this problem is designing a cost-effective, easy-to-maintain non-evasive CGM system. For this, electromagnetic (EM) based techniques were considered. When EM waves impinge on the human body, the reflected waves and emerged waves could be collected. These received and transmitted waves could be compared to

obtain information about several properties of human tissues. More precisely, any variations in the parameters of the received waves are directly related to the changes of the constitutive parameters of blood and the combination of this electromagnetic waves can be used to study several properties of human tissues. This variations in parameters of received signals can be directly correlated to blood glucose levels and this can be used for non-invasive monitoring.

A recent study by the World Economic Forum has suggested that continuous Glucose monitoring is one of the top ten emerging technologies and evolving towards non invasive smart wearable solutions that are pain less and needle free [5].

For glucose level monitoring in diabetic patients, there are three methods: (i) invasive (conventional), (ii) minimally invasive and (iii) non-invasive This thesis is focused on the third method, i.e. the non-invasive method. The RF - based noninvasive method requires an antenna to be used as an RF sensor. An RF sensor is an antenna system placed on the human body. The desired antenna characteristics for glucose concentration monitoring applications are good sensitivity, accuracy, wide bandwidth, and circular polarization.

1.2 Problems with Existing Devices

Non-invasive blood glucose monitoring devices have faced several challenges and limitations. Here are some common problems associated with existing non-invasive blood glucose monitoring devices [6-8]:

- **Accuracy:** One of the major challenges is achieving consistent and accurate glucose measurements. Non-invasive methods typically rely on indirect measurements, such as detecting glucose levels in sweat, interstitial fluid, or the skin, which can be less reliable compared to direct blood sampling. Factors like environmental conditions, skin type, device calibration, and individual variations can affect accuracy.
- **Calibration and individual differences:** Non-invasive devices often require calibration to

establish a correlation between the measured parameter (such as sweat or interstitial fluid glucose) and blood glucose levels. However, individuals may have different physiological responses, making it difficult to achieve accurate and consistent results for everyone. Calibration can also be cumbersome and time-consuming.

- **Limited availability and high costs:** While non-invasive glucose monitoring technologies have shown promise, many of them are still in the research and development phase or have limited availability. Some devices might be expensive, making them less accessible to a wider population.
- **Interference and variability:** Non-invasive methods may be affected by external factors, such as physical activity, temperature changes, or certain medications, leading to variability in the readings. This variability can make it challenging to rely solely on non-invasive devices for managing diabetes effectively.
- **Regulatory approval and acceptance:** Non-invasive blood glucose monitoring devices need to undergo rigorous testing and gain regulatory approval to ensure their safety and efficacy. The process of obtaining regulatory clearance can be time-consuming, and not all devices make it through the approval process. Additionally, healthcare professionals and individuals with diabetes may be skeptical of relying solely on non-invasive methods due to the aforementioned accuracy concerns.

It is important to note that technology is continually advancing, and new developments might have addressed some of these challenges. It's recommended to refer to the latest research and consult healthcare professionals for the most up-to-date information on non-invasive blood glucose monitoring devices.

1.3 Advantages of Microwave Measurement Techniques

Microwave measurement techniques have shown promise for non-invasive blood glucose measurement due to several potential advantages. While no technique is without limitations, microwave-based methods offer some unique features that make them a compelling option for non-invasive

glucose monitoring [9]. Here are some reasons why microwave measurement techniques are considered advantageous:

1. **Penetration Depth:** Microwaves have the ability to penetrate deeper into biological tissues compared to some other techniques like optical methods. This deeper penetration allows for measurements to be made closer to the blood vessels where glucose levels are more directly related. As a result, microwave techniques have the potential to provide glucose measurements that are more representative of the actual blood glucose levels.

2. **Minimal Sensitivity to Skin Variations:** Microwaves are less affected by skin characteristics and variations, such as skin color, texture, or thickness, compared to optical techniques. This reduced sensitivity to skin variations can help in achieving more consistent and accurate glucose measurements across different individuals, reducing the need for extensive calibration for different skin types.

3. **Reduced Interference from External Factors:** Microwave measurements are less affected by external factors like ambient light, temperature, and motion artifacts, which can be challenges for optical or thermal methods. This reduced interference can contribute to improved measurement accuracy and reliability.

4. **Rapid Measurement Time:** Microwave techniques typically provide relatively fast measurement times compared to some other non-invasive methods. The ability to obtain glucose readings quickly allows for more frequent monitoring and potentially more timely interventions for individuals with diabetes.

5. **Potential for Continuous Monitoring:** Microwave-based systems have the potential to enable continuous glucose monitoring, providing a real-time picture of glucose fluctuations throughout the day. This continuous monitoring can offer valuable insights into glucose trends and help individuals make more informed decisions regarding their diabetes management.

Chapter 2

Literature Survey

2.1 Necessity for continuous blood glucose monitoring

Continuous glucose monitoring (CGM) is an advanced technology that allows individuals with diabetes to continuously monitor their blood glucose levels throughout the day and night. It involves wearing a small sensor under the skin that measures glucose levels in the interstitial fluid and provides real-time data[10-13]. Here are some reasons why continuous blood glucose monitoring is considered necessary for certain individuals with diabetes:

1. **Real-time glucose monitoring:** CGM provides continuous and real-time data on blood glucose levels, enabling individuals to have a better understanding of their glucose patterns and trends. This information is valuable for making immediate adjustments to insulin doses, dietary choices, and physical activity to maintain optimal blood glucose control.

2. **Hypoglycemia detection and prevention:** CGM systems can help detect and alert users to impending hypoglycemia (low blood sugar) episodes. This is particularly important for individuals with a history of severe hypoglycemia or impaired hypoglycemia awareness. Timely alerts allow individuals to take necessary actions, such as consuming carbohydrates or adjusting insulin dosages, to prevent severe hypoglycemia.

3. **Hyperglycemia management:** CGM provides valuable insights into hyperglycemia (high

blood sugar) patterns, including post-meal spikes and overnight highs. By closely monitoring glucose levels, individuals can identify patterns, understand the impact of meals, and make appropriate adjustments to their insulin regimen or lifestyle choices.

4. **Reduced risk of complications:** Maintaining blood glucose levels within a target range is crucial for reducing the risk of diabetes-related complications. CGM helps individuals stay within their target range by providing continuous feedback and alerts when glucose levels go outside the desired range. By effectively managing glucose levels, the risk of long-term complications such as cardiovascular diseases, kidney problems, and nerve damage can be reduced.

5. **Improved quality of life:** CGM technology can enhance the quality of life for individuals with diabetes by reducing the burden of frequent fingerstick testing. CGM systems eliminate the need for multiple daily finger pricks, offering convenience and reducing discomfort associated with traditional glucose monitoring methods.

6. **Trend analysis and data insights:** CGM systems collect and store glucose data over time, allowing users to analyze trends, identify patterns, and gain valuable insights into their diabetes management. This information can be shared with healthcare providers to facilitate collaborative decision-making and adjustments to treatment plans.

CGM is not without its risks, however. Some of the risks of CGM include:

- **Sensor site reactions:** The sensor site may become irritated, red, or swollen.
- **Sensor failure:** The sensor may fail to send readings or may need to be replaced more often than expected.
- **Infection:** There is a small risk of infection at the sensor site.
- **Cost:** CGM is a more expensive way to monitor blood sugar than traditional methods such as fingerstick testing.

2.2 Techniques for blood glucose measurement

There are three main types of blood glucose measurement techniques: invasive, minimally invasive, and non-invasive [14-15].

1. **Invasive techniques** involve the insertion of a needle or catheter into the body to obtain a blood sample. This is the most accurate method of blood glucose measurement, but it can be painful and inconvenient. Invasive techniques include finger pricking, venous blood sampling, and arterial blood sampling. Finger pricking is the most common invasive technique for blood glucose measurement. It is a quick and easy way to obtain a blood sample, and it is relatively painless. Venous blood sampling is more accurate than finger pricking, but it is also more painful and inconvenient. Arterial blood sampling is the most accurate method of blood glucose measurement, but it is also the most invasive.

2. **Minimally invasive** techniques involve the insertion of a small sensor into the skin to measure blood glucose levels. This is less painful than invasive techniques, but it can still be uncomfortable. Minimally invasive techniques include continuous glucose monitoring (CGM) and flash glucose monitoring (FGM). CGM devices measure blood glucose levels continuously throughout the day. They are attached to the skin with a small sensor, and they transmit data to a receiver or smartphone. FGM devices are similar to CGM devices, but they only measure blood glucose levels every few minutes. They are less expensive than CGM devices, but they are also less accurate.

3. **Non-invasive techniques** do not involve the insertion of any needles or sensors into the body. These techniques are still in development, but they have the potential to be the most convenient and painless method of blood glucose measurement. Non-invasive techniques include near-infrared spectroscopy (NIRS), Raman spectroscopy, and photoacoustic spectroscopy. These techniques use light to measure blood glucose levels without the need for a needle or sensor. They are still in development, but they have the potential to be the most convenient and painless method of blood glucose measurement.

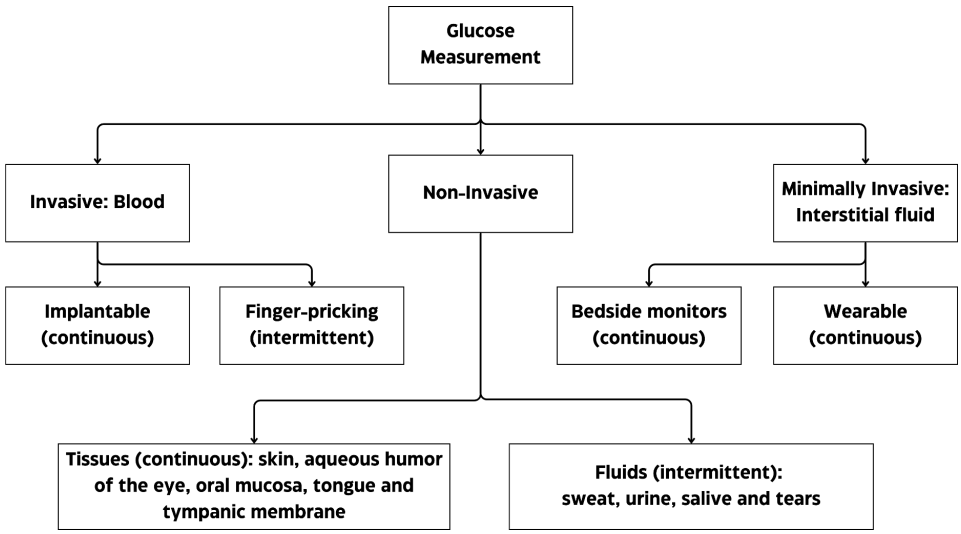


Figure 2.1: Techniques for blood glucose measurement

2.3 Non Invasive Blood Glucose Monitoring Devices

There are currently no FDA-approved non-invasive blood glucose monitoring devices on the market. However, there are a number of companies that are developing NIBGM devices [16-22]. Some of the most promising NIBGM devices in development include:

1. **Glucowise by Senseonics:** Glucowise is a wearable device that uses near-infrared spectroscopy (NIRS) to measure blood glucose levels through the skin. The device is still in development, but it has shown promise in clinical trials.

Figure 2.2: Glucowise by Senseonics

2. **Abbott FreeStyle Libre Flash by Abbott:** FreeStyle Libre Flash is a flash glucose monitoring (FGM) device that uses a small sensor inserted under the skin to measure blood glucose levels. The sensor can be worn for up to 14 days, and it does not require finger pricking.

Figure 2.3: Abbott FreeStyle Libre Flash by Abbott

3. **Nemaura Senso by Nemaura Medical:** Senso is a non-invasive blood glucose monitoring device that uses Raman spectroscopy to measure blood glucose levels through the skin. The device is still in development, but it has shown promise in clinical trials.

Figure 2.4: Nemaura Senso by Nemaura Medical

4. **C8 MediSensors by C8 MediSensors:** C8 MediSensors is a non-invasive blood glucose monitoring device that uses photoacoustic spectroscopy to measure blood glucose levels

through the skin. The device is still in development, but it has shown promise in clinical trials.

Figure 2.5: C8 MediSensors by C8 MediSensors

These are just a few of the many NIBGM devices that are currently in development. It is likely that we will see more NIBGM devices on the market in the coming years.

It is important to note that NIBGM devices are still in development, and they are not yet as accurate as traditional methods of blood glucose measurement. However, there is a lot of promise for NIBGM devices, and they have the potential to revolutionize the way that blood glucose is measured.

Following drawbacks are observed in the existing Non Invasive continuous blood glucose monitoring devices like high cost, not comfortable to wear continuously throughout the day & requires lots of maintenance [23-33]. In table 2.1 few existing continuous blood glucose measurement devices are compared based the Measurement site , working principle and type of measurement done. Based on table 2.1, it is clear that the existing devices make use of sensors which needs to be replaced and are costly and cannot be wore for extended period of time.

Table 2.1: Continuous Blood Sugar Measurement Representative

Device Name	**Measurement Method**	**Measurement Principle**	**Measurement Type**	**Year**
D-SaLife	Saliva (tongue) probe	Micro Current Control	Non-Invasive	2021
Biolinq	Skin Patch	Electrochemical Biosensor	Minimally Invasive	2019
Dexcom G6	Abdominal Patch	Electrochemical Biosensor	Non-Invasive	2018
Symphony	Skin Patch	Electrochemical Biosensor	Non-Invasive	2011
Freestyle Libre 2	Bicep Skin Patch	Electrochemical Biosensor	Non-Invasive	2020
Eversense	Under the arm implant	Electrochemical Biosensor	Minimally Invasive	2018
Noviosense	Upper Eyelid	Electrochemical Biosensor	Minimally Invasive	2017
Google Smart Lens	Retina	Electrochemical Biosensor	Minimally Invasive	2015
Combo Glucometer	Finger	Infrared Spectroscopy	Non-Invasive	2014
GlucoTrack	Ear Lobe	Ultrasound + thermal + electromagnetic	Non-Invasive	2017
SugarBEAT	Upper Arm	Reverse Iontophoresis	Minimally Invasive	2017

2.4 Comparison of method of CGM

From the published literature it has been found that there are a number of Continuous Blood Glucose measurement techniques that are under development. All this measurement techniques offer a number of advantages over traditional finger prick methods. The comparison is presented in table 2.2 which describes the working principle pros and cons of the existing Non Invasive Blood glucose measurement techniques [34-39].

1. **Optical Techniques:** These methods utilize light to measure glucose levels. They include techniques such as transcutaneous absorption spectroscopy, diffuse reflectance spectroscopy, and near-infrared spectroscopy. These techniques analyze the interaction of light with tissues to estimate glucose concentrations. Challenges in optical techniques include interference from other substances and limited penetration depth.

2. **Thermal Techniques:** Thermal-based methods measure changes in skin temperature caused by variations in blood glucose levels. These methods include thermography and infrared thermometry. They rely on the principle that glucose metabolism affects skin temperature. However, factors like environmental conditions and local blood flow can influence accuracy.

3. **Impedance Spectroscopy:** This technique involves passing a low-intensity electric current through the skin and measuring the resulting impedance changes. Glucose concentration influences the electrical properties of tissues, allowing for glucose estimation. Challenges include electrode-skin interface variability and the need for calibration.

4. **Raman Spectroscopy:** Raman spectroscopy analyzes the scattered light from tissues to identify glucose levels. It measures molecular vibrations and provides specific glucose-related information. However, this technique is sensitive to motion artifacts and requires complex data processing.

5. **Acoustic Techniques:** These methods assess changes in tissue properties using ultrasound or acoustic signals. For example, ultrasonic backscattering techniques correlate changes in

Table 2.2: Comparison of non-invasive blood sugar measurement techniques

Method	**Working Principle**	**Pros**	**Cons**
Optical Polarimetry	Polarization of light beam by glucose molecule is measured	Easy to reduce size of optical components	Interference from other optical sources can change results
Optical coherence tomography	Light reflected by skin is fed to interferometer and refractive index of light is proportional to sugar concentration	Measurement is not affected by blood pressure or heart rate	Sensitive to skin temperature
Florosence	Stoke's shift in fluorophores is measured	Highly accurate and immune to light scattering	Sensitive to breathing rate
Surface Plasmon Resonance (SPR)	Changes in sugar concentrations causes changes in refractive index and relatively shift in the resonant frequency	Highly accurate	Sensitive to skin temperature and motion
Near Infrared Spectroscopy (NIR)	Absorption and scattering of wavelengths in the 780 nm to 2500 nm range	Immune to interfering surfaces	High light scattering possibility
Microwave Sensing	Amplitude and phase variation of scattering parameters of antenna	Deep penetration directly to the artery and vein	Age and gender specific calibration is required

backscattered ultrasound signals with glucose levels. Challenges include limited accuracy and interference from tissue heterogeneity.

6. **Continuous Glucose Monitors (CGMs):** CGMs are invasive devices, but some emerging technologies aim to make them non-invasive. These methods utilize sensors placed on the skin surface, such as microneedles or patches, to measure glucose levels in interstitial fluid. While these are not completely non-invasive, they offer a less invasive alternative to traditional finger-prick testing.

Each technique has its advantages and limitations, and their accuracy and reliability vary. Overcoming challenges related to accuracy, calibration, interference, and user-friendliness remains a focus of ongoing research and development in non-invasive blood glucose measurement.

2.5 Validation of Results using Clarke Grid Model

The Clarke Error Grid has been analysed as benchmark tool to examine the clinical precision for biomedical application [40]. It has prediction of point as well as rate accuracy, and it amends for physiologic time lags inherent for measurement of body glucose.

	Clarke Error Grid [ ]	Parkes Error Grid Type 1 Diabetes [ ]	Parkes Error Grid Type 2 Diabetes [ ]	Surveillance Error Grid [ ]
Risk zones	A to E	A to E		Green to Dark-red
A Green	Clinically correct decisions	No effect on clinical action		No risk
B G/Y	Clinically uncritical decisions	Altered clinical action or little or no effect on clinical outcome		Mild risk
C Y/R	Overcorrections that could lead to a poor outcome	Altered clinical action: likely to affect clinical outcome		Moderate risk
D Red	Dangerous failure to detect and treat	Altered clinical action: potential significant medical risk		High risk
E Dark Red	Erroneous treatment	Altered clinical action: potential dangerous consequences.		Extreme risk

Figure 2.6: Standard error grids for clinical accuracy assessment of glucose detection

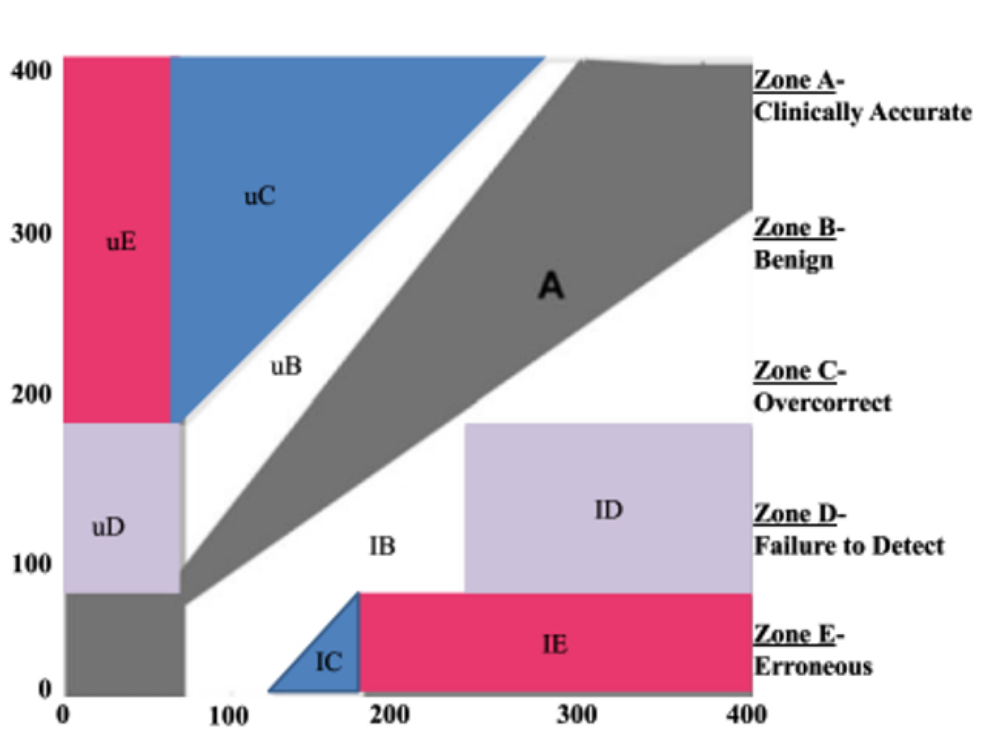


Figure 2.7: Zones of assessment of blood glucose

Chapter 3

Research Objectives

This thesis has the main objective to design and fabricate various microstrip patch antennas that can be used as RF sensors for non-invasive blood glucose monitoring. In this thesis, the main focus is to develop highly sensitive and accurate RF sensors. The primary objectives are as follows:

- To Design and develop suitable Microwave Sensor that would be utilized for Non Invasive Blood Glucose Sensing
- To demonstrate correlation between di-electric properties of blood & Blood Glucose Level
- To design Multilayer equivalent Human Arm Model based on di-electric properties of layers of human Arm tissue
- To perform Non Invasive experiments on human subjects using microwave sensor

Chapter 4

Contribution

4.1 Human Model

4.1.1 Human Arm Model Design using Cole Cole Equation

General steps followed while deriving the target-specific human body model for simulation and design of non-Invasive blood glucose measurement system shown in figure 4.1. Once the equation derivation was done, only the human forearm model was designed and properties are assigned to it, instead of the full-body model. The detailed discussion and flowchart for this model design are shown in figure 4.2. If we want to measure blood sugar at the heart or stomach or ear or forearm, the body model will vary accordingly. But the steps explained in figure 4.2 will stay the same. Since target is the human forearm, so we need to consider its anatomy. The human forearm has two supporting bones, one major artery and one major vein apart from fats and muscle layers. This model and its calculation will change if we want to measure blood glucose in the stomach. We also need to decide the frequency range of interest at the start of derivation so that model or mathematical derivation could be done for a narrowband or wideband. The selection of suitable models like the Cole-Cole or Debye model will depend upon the end application. In the intended application, measurement of electrical conductivity is important, hence, we have selected the Cole-Cole equation model.

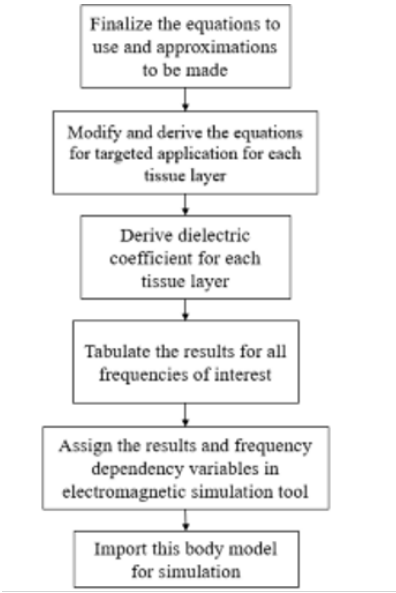

Finalize the equations to use and approximations to be made
Modify and derive the equations for targeted application for each tissue layer
Derive dielectric coefficient for each tissue layer
Tabulate the results for all frequencies of interest
Assign the results and frequency dependency variables in electromagnetic simulation tool
Import this body model for simulation

Figure 4.1: General steps followed for the design of human body model

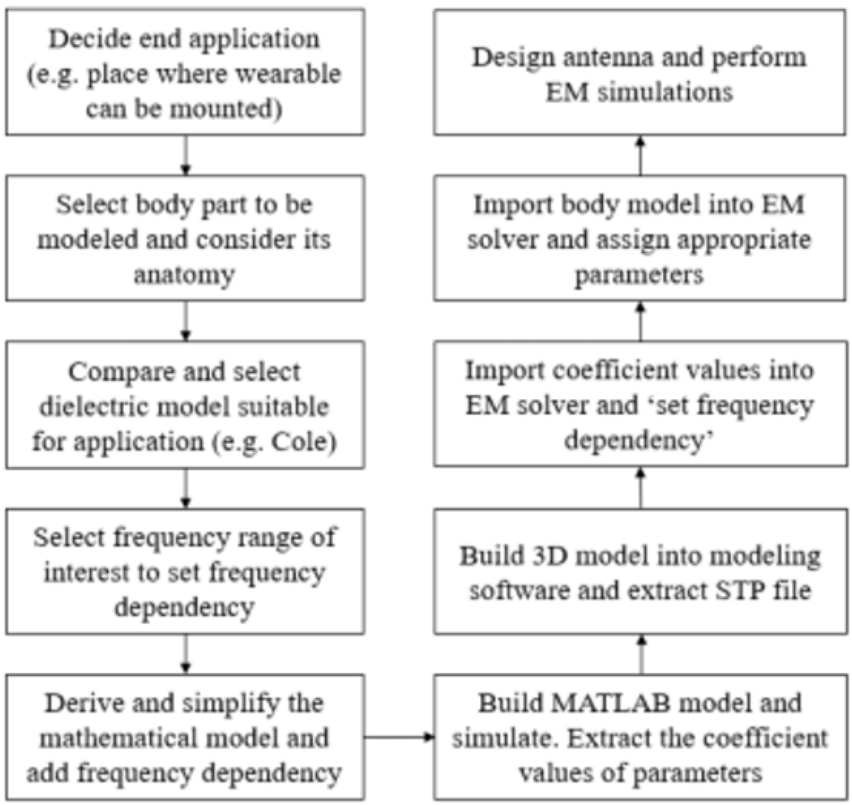

Decide end application (e.g. place where wearable can be mounted)
Select body part to be modeled and consider its anatomy
Compare and select dielectric model suitable for application (e.g. Cole)
Select frequency range of interest to set frequency dependency
Derive and simplify the mathematical model and add frequency dependency
Build MATLAB model and simulate. Extract the coefficient values of parameters
Build 3D model into modeling software and extract STP file
Import coefficient values into EM solver and 'set frequency dependency'
Import body model into EM solver and assign appropriate parameters
Design antenna and perform EM simulations

Figure 4.2: Flowchart used to build required human hand model

The final frequency dependent Cole -Cole equation can be written as:

$$(\varepsilon(\omega)) = Re[\varepsilon_\infty + \Sigma\frac{\Delta\varepsilon}{(1+j\omega\tau)^{(}1-\alpha)}.[(0.001445G) + 1.145382]] + Im[\varepsilon_\infty + \Sigma\frac{\Delta\varepsilon}{(1+j\omega\tau)^{(}1-\alpha)} + (\frac{\rho}{j\omega\varepsilon_0})]$$

The Cole model was selected for derivation since material conductivity is a useful parameter here. All the symbols used in derivation are shown in Table 4.2 below.

Table 4.2: Symbols used in Cole Model

Symbol	Meaning
$\varepsilon^{'}$	Real part of dielectric constant
$\varepsilon^{"}$	Imaginary part of dielectric constant
ρ	Volume
σ	Electrical Conductivity
A	Attenuation constant of the wave
B	Phase constant of the wave
Ω	Angular velocity of the wave

To characterize these equations and related parameters, MATLAB program was built and used for obtaining further data, as given in subsequent sections of this paper. An important point to note here that when the model was designed in ANSYS HFSS, all physical measurements and related parameter values were considered for an adult male in the age range of 35-45 years. The target system of for non-invasive blood glucose measurement needs to estimate the interaction of antennas with the human body. For such type of estimation, the channel model between transmitter and receiver is the human hand which has been discussed in the previous section.

Other relevant physical parameters are given as in table III. We also used anthropologic data for physical modeling [22], the values are shown in Table 4.2.

Table 4.3: Relevant physical parameters for modelling the human hand

Tissue	**Density (kg/m^3)**	**Conductivity (S/m)**	**Dielectric Constant**	**Loss Tangent**	**Penetration Depth (mm)**
Blood	1050	2.5024	58.347	0.31123	0.016407
Blood vessel	1075	1.4041	58.347	0.31123	0.016407
Fat	911	0.10235	5.2853	0.14503	0.11956
Muscle	1090	1.705	52.791	0.24191	0.022785
Bone Cortical	1908	0.38459	11.41	0.25244	0.046992
Skin	1109	1.4407	38.063	0.2835	0.022956

The Cross-section of the hand model is shown in figure 4.3. Each tissue layer is being treated as a dielectric material. When multiple dielectric materials are put together in a certain combination and a radio signal is passed through this arrangement, it is important to know its equivalent circuit.

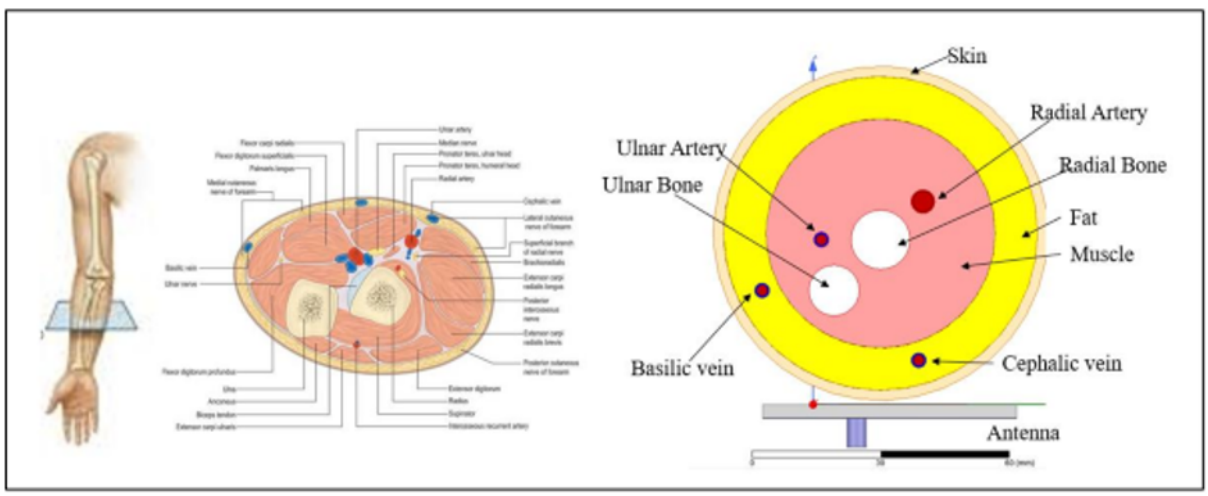


Figure 4.3: Designed Model Cross Section

To validate the model simple antenna was taken from [41]. This antenna is a circular patch

Table 4.4: Physical measurements of human hand

Human Tissue	**Measure (mm)**	**Description**
Skin	2.45	Thickness of the dermal tissue
Fat	12	Thickness of the fat layer below dermal tissues
Cephalic Vein	1.9	Outer diameter of the major vein
	1.7	Inner diameter of the major vein
Basilic Vein	1.8	Outer diameter of major vein
	1.6	Inner diameter of the major vein
Ulnar Artery	1.8	Outer diameter of the major artery
	1.6	Inner diameter of the major artery
Radial Artery	4.5	Outer diameter of the major artery
	4.2	Inner diameter of the major artery
Radial Bone	11	Averaged diameter when shape normalized to circular cross-section
Ulnar Bone	7	Averaged diameter when shape normalized to circular cross-section
Muscle	24	Thickness of the fat layer below fat layer

antenna with a copper wrist band that acts as a ground. To evaluate the model, we had tried to change the glucose concentration of the blood plasma in the proposed model by varying its electrical conductivity and dielectric constant. These values can be seen in Table 4.3. Each time the values are changed, the simulation was run and variation in antenna return loss was monitored as the first measure.

Finally, the SAR plot for this model was also done and found to be well below FCC limits. The SAR plot is shown in figure 4.5. SAR value depends on the internal electric field generated in the body and can be given as,

$$\text{SAR}=\frac{\sigma E^2}{\rho}$$

Some volunteers were used for verification of these results. It was also ensured that some

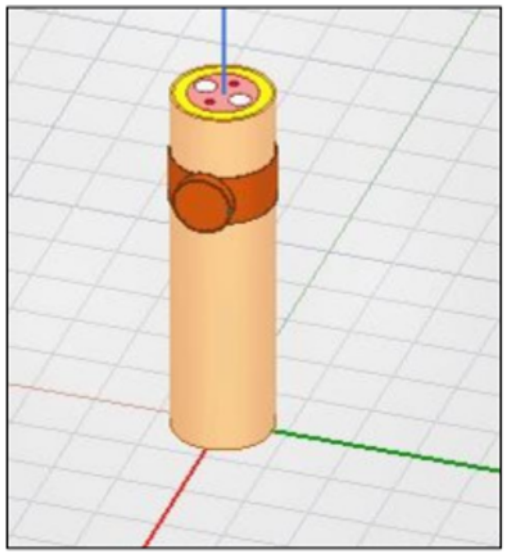


Figure 4.4: Location of designed antenna on human wrist

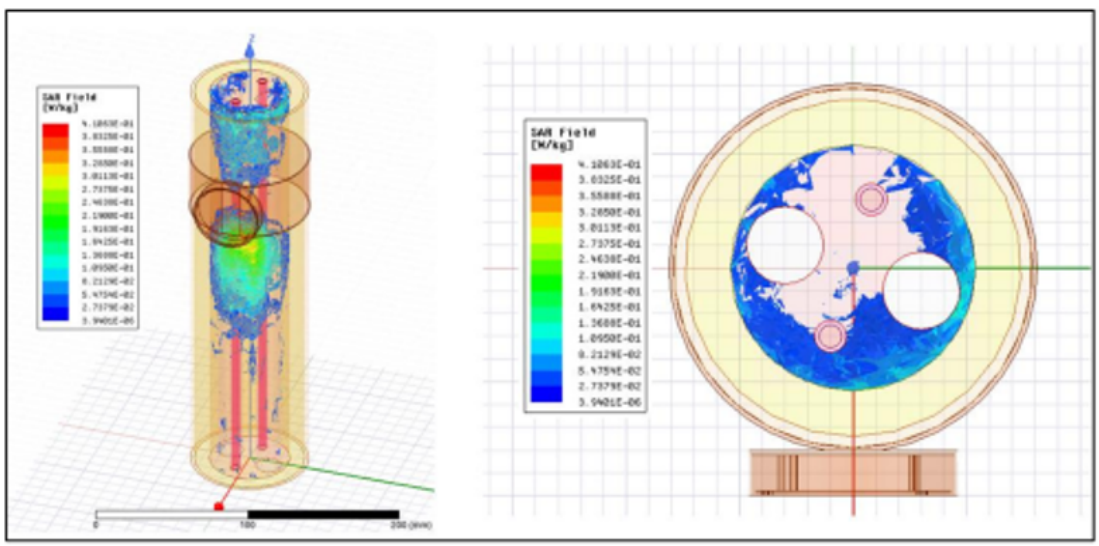


Figure 4.5: SAR Plot

Table 4.5: Variation in antenna performance based on blood glucose variation

Glucose (mg/dL)	**Frequency (GHz)**	**Dielectric Constant (Blood Plasma)**	**Conductivity (S/m)**
70	2.4	58.3212	2.5122
220	2.4	58.1257	2.4525
340	2.4	58.0025	2.3994
600	2.4	57.8994	2.3569

volunteers have known diabetic conditions and the remaining were non-diabetic. The following steps are used to compare simulation results with measurement results:

- Fabricated antenna performance was measured with all volunteers on a network analyzer. Return loss values were recorded.
- For the same volunteers, glucose levels were measured with standard finger pricking techniques. These values were also recorded.
- These measured glucose concentration values were put in a mathematical model derived in section III to obtain parameter values for simulation. Simulations were carried out and simulated return loss values were recorded.
- Hence, for the same glucose concentration values, simulated vs measured return loss was compared to establish the accuracy of the proposed model. The results are plotted in figure 4.6. It can be seen from the results of figure 16 that glucose measurement accuracy with the proposed method for extreme lower and extreme higher ends of blood-glucose concentrations is less, as return loss variation ranges in the 4 to 6 dB range. The blood-glucose concentration within the range of 170 mg/dL to 450 mg/dL is within the range of 1 to 3 dB. Simulated and measured results are also in agreement with the mentioned blood-glucose ranges.

The proposed human body model has a feature to change blood glucose concentration and track the changes in antenna performance. This human body model was designed keeping in mind the

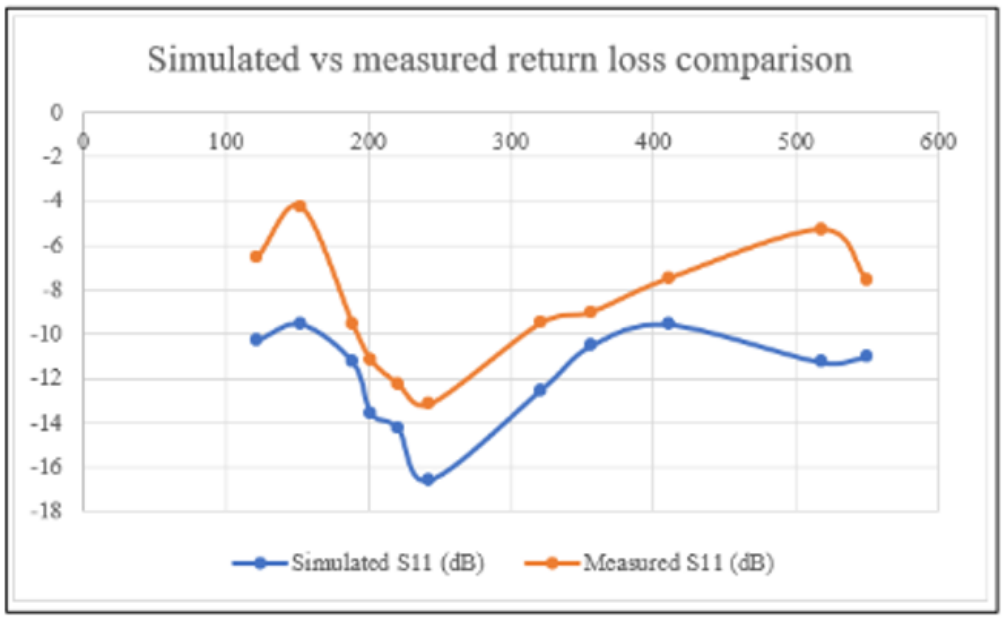


Figure 4.6: Location of designed antenna on human wrist

male body of age group between 35-45 years of ages and Indian ethnicity. From the mathematics presented here and the proposed model, it has been shown that any changes in the blood glucose concentration directly affect the antenna performance. Also, a relation between antenna performance variation against the blood glucose concentration change can be established.

It was found that blood glucose variation on the extreme ends of the glucose concentration has return loss variation in the ranges of 4 to 6 dB, while in the middle range (from approximately 170 mg/dL to 450 mg/dL) blood glucose variation ranges between 1 to 3 dB values. These major objectives have been proved in this paper. SAR for the proposed model was plotted and found to be well within the limits. Future work will involve testing the antenna performance variation based on different age groups and genders for further optimizing the antenna.

4.2 Antenna Design

4.2.1 Existing Antenna

We had studied and compared various wearable antennas proposed through the literature. A comparison of smartwatch antennas is given in table 2.2.

Table 4.6: Types of antennas proposed in the literature

Antenna Type	**Substrate**	**Dimensions (sq.mm)**	**Gain (dB)**	**Return loss (dB)**	**Ref**
Microstrip fed fractal	FR4, 1.6mm	28x24	0.5	-22	42
E shaped dipole	Denim (Er=1.7)	62x46	1.26	-12	43
Slotted patch	Textile	43x49	5.93	-20	44
Slotted patch	Denim	62.2x31.2	6.26	-18	45
Square patch	Air	1.8x3	5	-11	46
Circular patch	Air	44.8mm (diameter)	3	-20	47
Printed monopole	FR4, 1.6mm	17.4mm (diameter)	0.5	-23	Proposed

The major limitation with all the antennas is that the cannot be retuned once fabricated

4.2.2 Antenna Design Evolution

The antenna evolution takes place through 4 iterations.

1. Iteration 1

   In the first iteration a simple monopole antenna with coaxial feed is designed and tuned for desired frequency. The printed monopole is shorted to the ground. The markers indicate the feed positions which can be used to retune the antenna. The major limitiation with this structure is the size of antenna.

   Monopole Patch antenna calculations

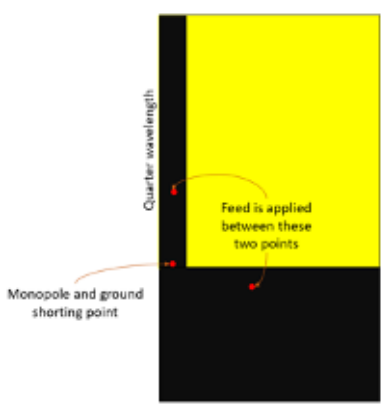


Figure 4.7: (Simple Monopole Antenna Tuned at 2.4 GHz.

2. Iteration 2

   In this iteration the quarter wavelength monopole antenna is folded to reduce the antenna dimensions.This antenna has comparatively less gain than 1st iteration but its performance is stable in air.

3. Iteration 3

   In this iteration the antenna structured is modified in such a way that it can fit inside the round shaped smart watch dial.The length of circular arm matches the length of Monopole. In this iteration the return loss is improved but there is significant reduction in the gain.

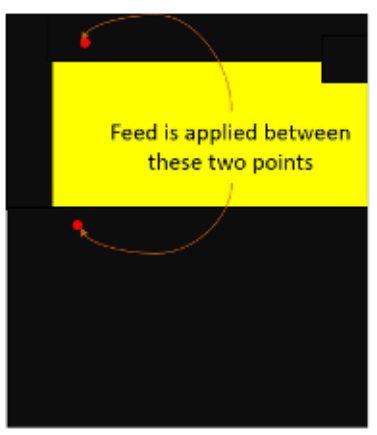


Figure 4.8: Quarter wavelength monopole folded to Square Dial Structure.

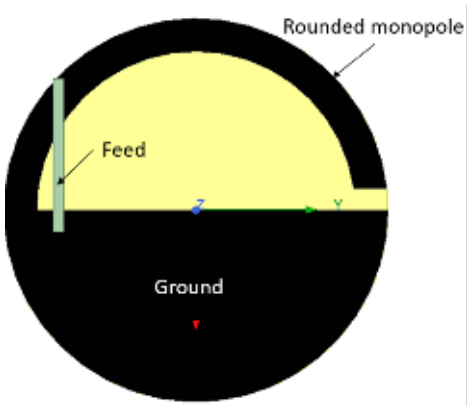


Figure 4.9: Monopole rounded to fit into smartwatch dial.

4. Iteration 4

   This is the final iteration structure in which structure of top layer is same as iteration 3 but the ground plane from top layer is replicated in bottom layer.Both this layers are connected to each other through series of vias.

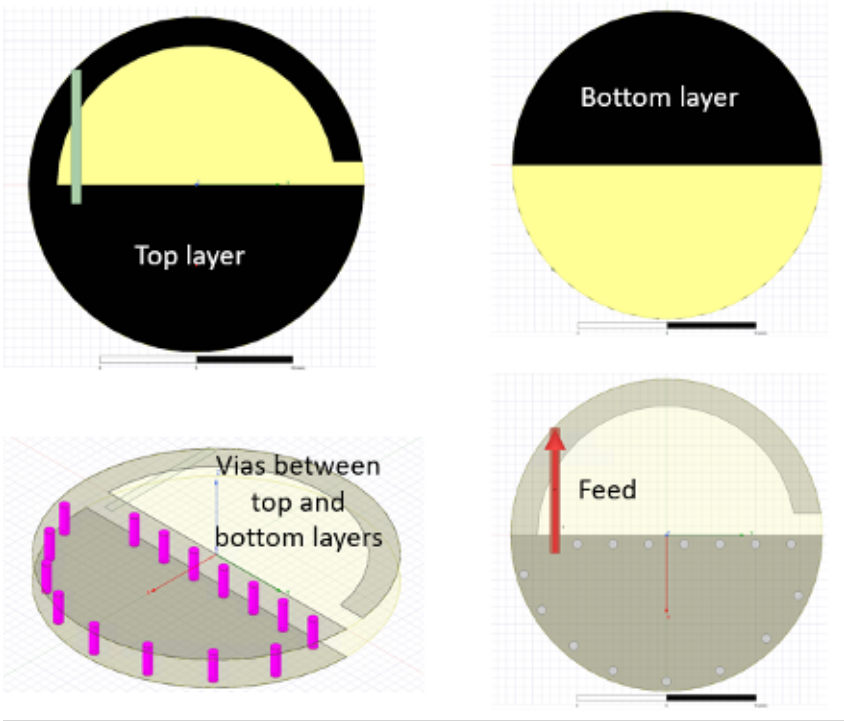


Figure 4.10: Antenna design evolution.

Figure 4.10 shows the structure of final antenna in detail with via placement and feed location. Top and bottom layers show the copper part. Figure 3(d) shows port allocation and current distribution on the antenna surface.

4.2.3 Simulation and Fabrication Results

Figure 4.10 shows the structure of final antenna in detail with via placement and feed location. Top and bottom layers show the copper part. Figure 4.10 shows port allocation and current distribution on the antenna surface.

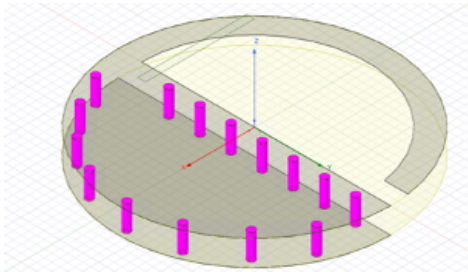


Figure 4.11: Structure details (a) via arrangement between top and bottom

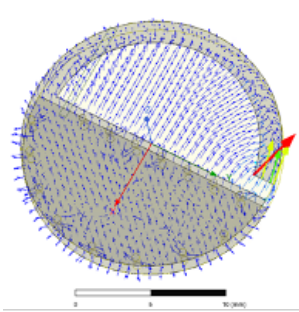


Figure 4.12: Structure details (b) surface current at 2.4 GHz

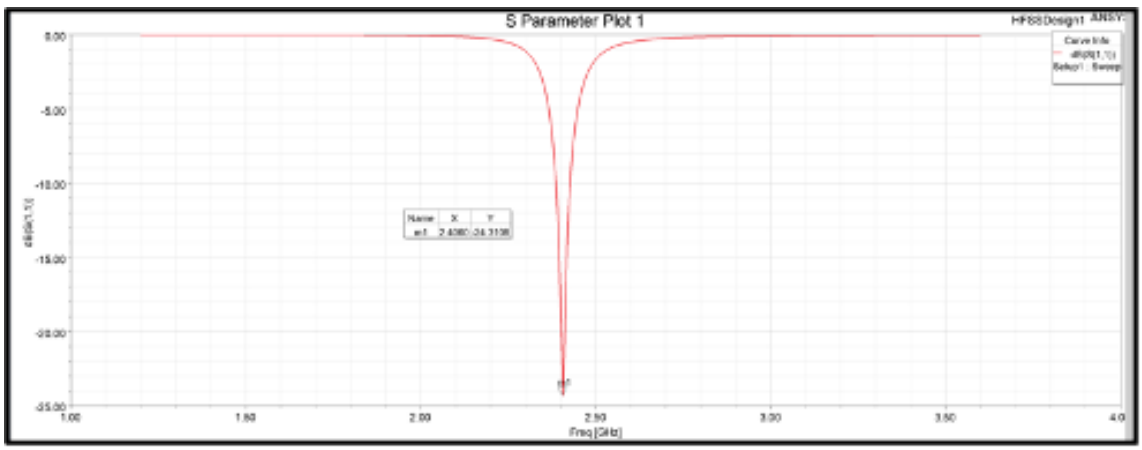


Figure 4.13: Return loss of the final iteration A4

The return loss of -24dB is observed in simulation and gain of 0.5dB with VSWR value of 1.2 in the final Antenna structure. Also, by increasing or decreasing the length of rounded arm, this antenna can be retuned.

Table 4.7: Final Antenna Results

Parameter	**Unit**	**Value**
Antenna type	NA	Printed rounded monopole
Dimensions	mm	Circular, dia. = 40
Substrate		FR4 epoxy
Dielectric constant		4.4
Height	mm	1.6
Conductor		Aluminium

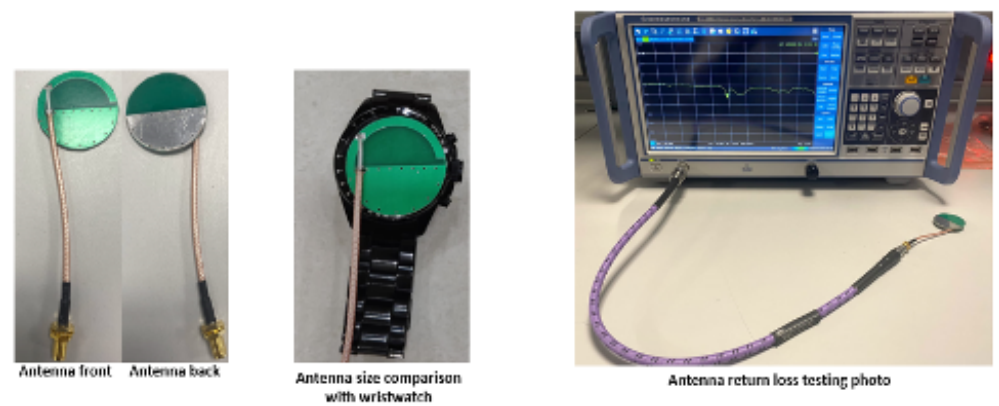


Figure 4.14: A4 fabricated and tested (a) top and bottom layers of fabricated antenna (b) antenna size comparison with regular wristwatch dial (c) antenna test photograph for return loss measurement

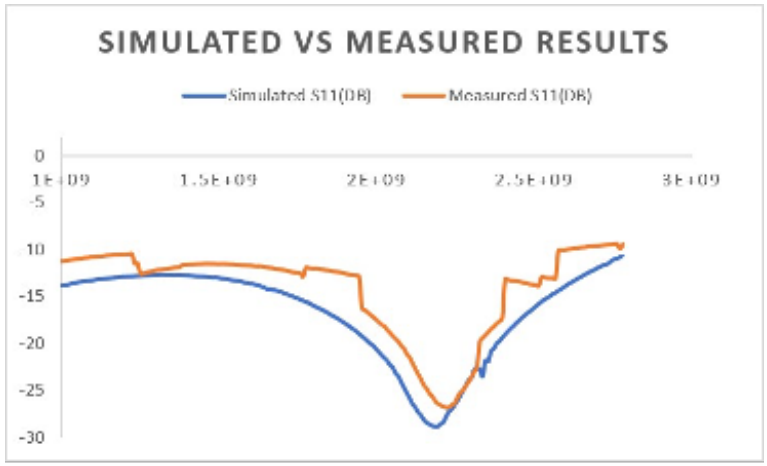


Figure 4.15: Antenna measurement result

4.3 Final System Integration

Though the final system integration can include microcontroller and memory unit, we have used vector network analyser and direction coupler to evaluate the designed prototype. For any resonant frequency, we can measure the changes in antenna return loss (S11) due to blood glucose variation using this setup. The measurement setup requires continuous wave (CW) signal source, directional coupler and VNA. Figure 14 shows the basic measurement setup for this connection. At the time of final integration with smartwatch, surface mounted, or chip-based directional coupler can be used.

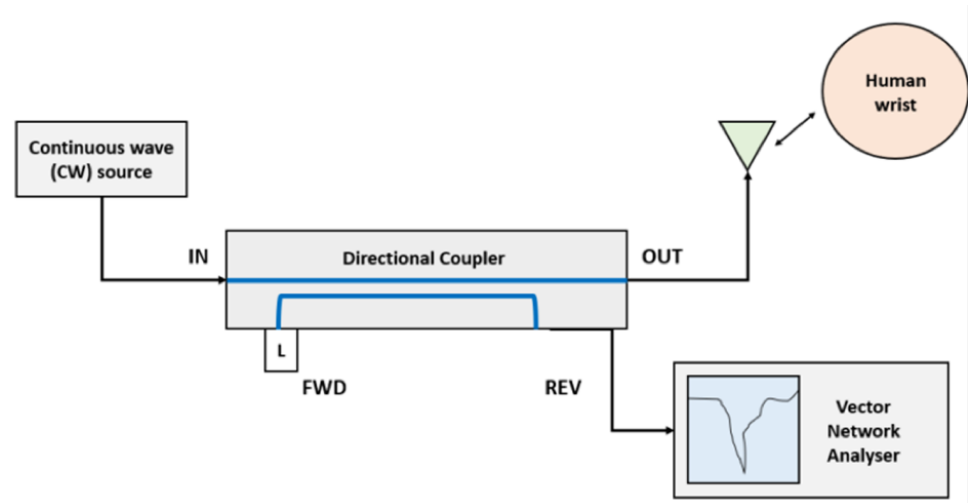


Figure 4.16: Basic measurement setup for the lab

Directional coupler plays an important role in the measurement and hence, it will also be used in final system integration. Directional coupler working is explained in figure 8 for the intended measurement. Experimental Setup used 10 dB directional coupler with directivity 25 dB and insertion loss of 0.45 dB.

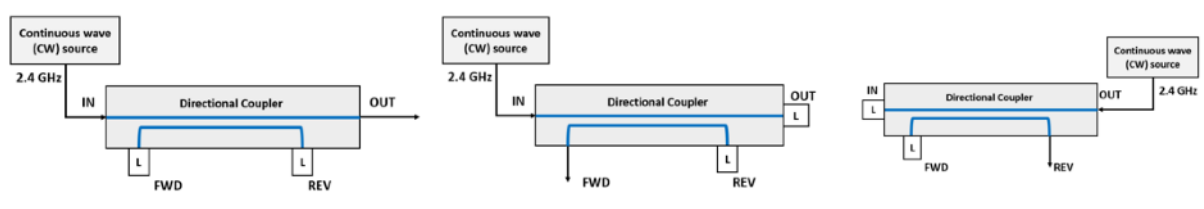


Figure 4.17: Directional coupler basic working and connection diagram

Antenna S11 variation due to blood glucose change will not be significant, the power variation could be in mW or micro-W but that depends on power being fed into antenna ports. For measurement purposes, 3 dBm input power is fed through directional coupler to antenna inputs to obtain detected voltage change in mV range. Below figure 15 shows example calculation at mW calculation changes. Using directional coupler improves the system accuracy. Using the setup in figures 14 and 15, blood glucose values from aqueous solution have been calculated . This measurement was carried out initially, and the obtained values are listed in table 1 .

Table 4.8: Blood glucose values measured from aqueous solution.

Sr. No.	**Aqueous solution concentration (mg/dL)**	**Estimated concentration with setup of fig.9 (mg/dL)**
1	72	78
2	86	94
3	99	108
4	137	141
5	257	262

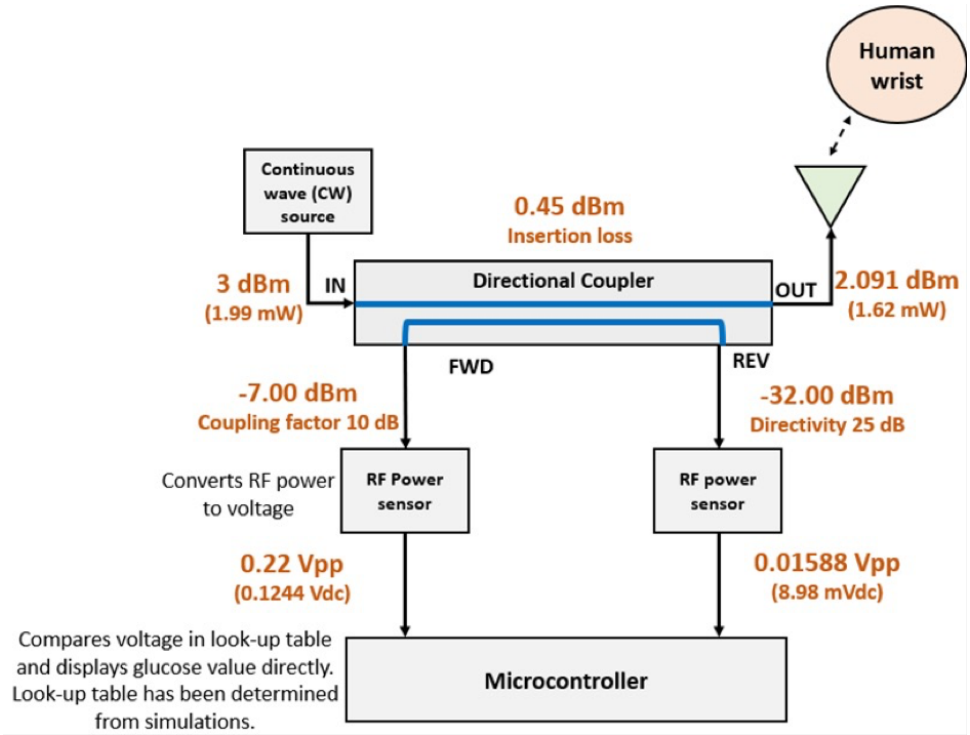


Figure 4.18: Sample calculation about how return loss variation translates into blood glucose value

It is observed from table 4.8 that results are fairly accurate, however, authors wanted to verify the results with finger pricking method. For this purpose, authors collaborated with a diagnostic lab and conducted a blood glucose measurement drive at the lab. Blood glucose samples from few volunteers where collected using conventional finger pricking measurement as well as using measurement setup explained in figures 14 and 15, simultaneously. The results of measurement are listed in table 10. Measurement photograph is shown in figure 17 and fabricated prototype is shown in figure 18.

It can be observed from table 2 that at the lower end of blood glucose concentration, estimation is fairly accurate with difference of 2-5 mg/dL. However, at the higher end of blood glucose concentration the difference between finger pricking based detection and proposed system-based detection is high ranging between 7-15 mg/dL. Clarke error grid is plotted to evaluate the proposed system performance, as shown in figure 18.

It can be seen from Clarke error grid model that the proposed system can accurately estimate

Figure 4.19: A representative measurement photograph

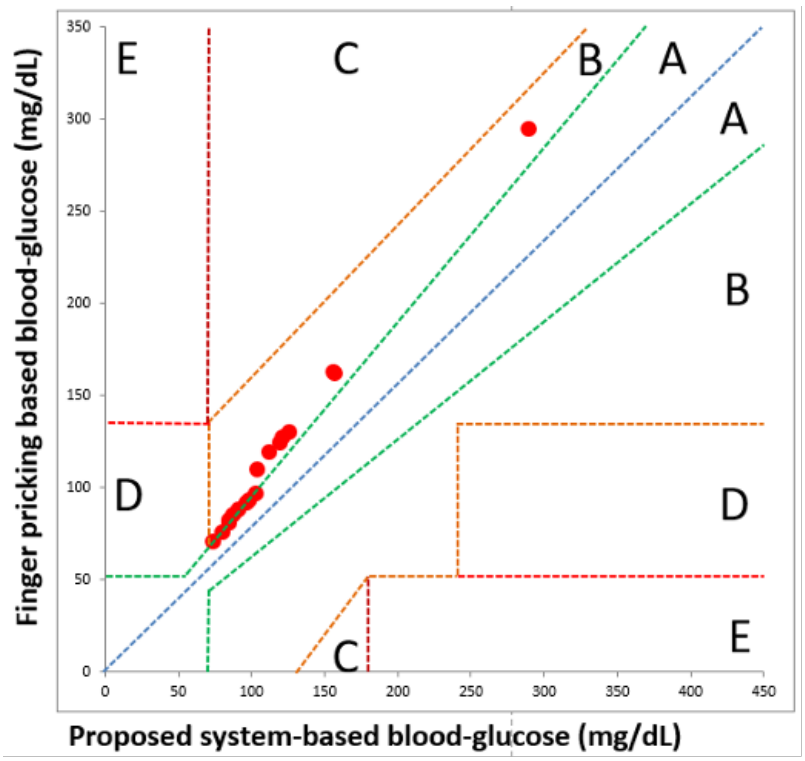


Figure 4.20: Blood glucose concentrations tabulated in table 2 are plotted on Clarke error grid.

Table 4.9: Proposed system measurement results vs finger pricking measurement.

Volunteer Number	**Gender**	**Age (Years)**	**Finger pricking based blood-glucose (mg/dL)**	**Proposed system-based blood-glucose (mg/dL)**
1	Female	40	84.54	82
2	Male	66	102.90	97
3	Male	17	87.86	85
4	Male	56	126.09	130
5	Male	65	156.98	162
6	Male	66	80.50	76
7	Female	30	96.48	92
8	Male	67	289.30	295
9	Female	65	84.54	81
10	Male	57	97.96	93
11	Female	38	73.28	71
12	Female	74	104.02	110
13	Male	30	112.06	119
14	Female	49	91.46	88
15	Male	66	119.34	124
16	Female	63	156.24	163
17	Female	50	121.39	127

the real-time blood glucose value. Also seen from figure 19, the absolute difference points between traditional and proposed system method of real time blood glucose measurements. This gives fair idea of accuracy of the system proposed in this work.

The same process was carried out for 200 Volunteers and correction factor is proposed for

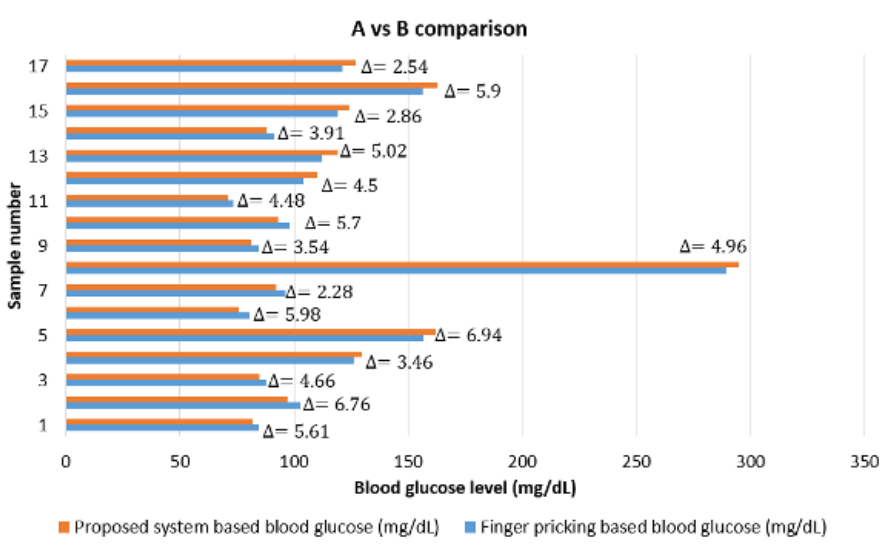


Figure 4.21: Absolute difference and A vs B comparison of traditional method vs proposed system for blood glucose measurement.

different blood glucose levels.

Measurement factor is proposed as,

$$\text{Measurement error} = \{g_m(t) - [g_a(t).b(t).R]\}$$

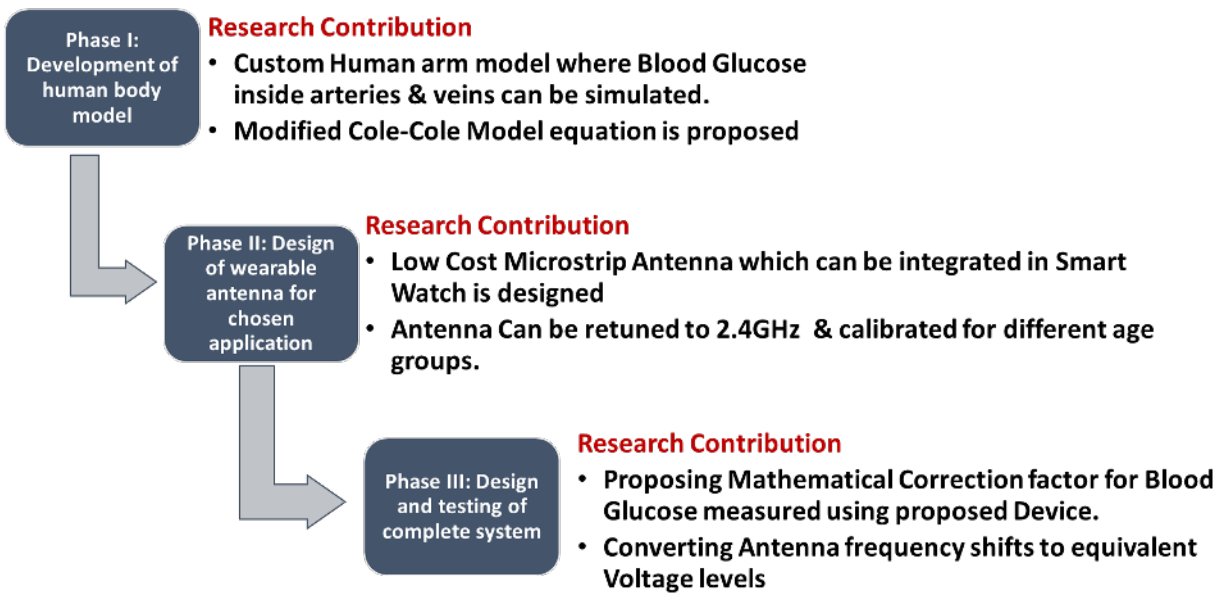
Table 4.10: Symbols and their meanings

$g_m(t)$	measured blood glucose level with proposed system
$g_a(t)$	actual blood glucose level with traditional invasive method
b(t)	body factor that depends on the meal timings
R	determined from lab tests and its value varies for ranges of glucose levels; it is 3.5 when glucose in the range 50-80 mg/dL, 1.5 when blood glucose ranges from 80-120 mg/dL and 11 when blood glucose ranges from 120-350 mg/dL

It was also noted that on lower values of blood glucose (below 80 mg/dL), proposed system has tolerance of 2-5 mg/dL irrespective of gender. However, for higher values of blood glucose (above 100 mg/dL) the proposed system has tolerance of 7-15 mg/dL.

Chapter 5

Conclusion


Phase I: Development of human body model
Research Contribution
• Custom Human arm model where Blood Glucose inside arteries & veins can be simulated.
• Modified Cole-Cole Model equation is proposed
Phase II: Design of wearable antenna for chosen application
Research Contribution
• Low Cost Microstrip Antenna which can be integrated in Smart Watch is designed
• Antenna Can be retuned to 2.4GHz & calibrated for different age groups.
Phase III: Design and testing of complete system
Research Contribution
• Proposing Mathematical Correction factor for Blood Glucose measured using proposed Device.
• Converting Antenna frequency shifts to equivalent Voltage levels

The entire project work is divided into 3 phases and the conclusion drawn are as follows

- Phase 1 Development of Human Body Model

  A customised human arm model is developed which can be configured to specific blood glucose values. Modified Cole cole equations are proposed which can be used to characterisie biological tissues. The designed human model was developed considering actual anatomy and anthropologial data.The Developed human model was validated by fabricating on an-

tenna and return loss was calculated for different values of Blood glucose levels.

It was found that blood sugar variation on the extreme ends of the glucose concentration has return loss variation in the ranges of 4 to 6 dB, while in the middle range (from approximately 170 mg/dL to 450 mg/dL) blood glucose variation ranges between 1 to 3 dB values. SAR for the proposed model was plotted and found very less as compared to standard 1.6w/kg..Thus in this work a customized Human Arm Model was implemented which has a provision to change blood glucose parameters which can be used for electromagnetic Simulations.

- Phase 2 Antenna Design Conclusion

  An electrically small wearable tunable antenna that could conform to a smartwatch dial is implemented. This antenna is having a provision of Retuning back to 2.45 Ghz which allows measurement of Blood Glucose on different Human arms and the detuned antenna can be retuned and calibrated easily.

- Phase 3 Final System Integration & Testing

  The fact that change in blood glucose concentrations changes dielectric properties of blood and This change can be estimated with an antenna was successfully verified. Antenna Return loss was measured with aqueous solution and later with volunteers in clinical trials. It was found that glucose concentrations estimated with antennas agree with simulation results as well as the finger pricking based results. It was also noted that on lower values of blood glucose (below 80 mg/dL), proposed system has tolerance of 2-5 mg/dL irrespective of gender. However, for higher values of blood glucose (above 100 mg/dL) the proposed system has tolerance of 7-15 mg/dL. Finally the validation was carried out with the help of Clarke grid model & statistical test and results where found to be 95% accurate.A mathematical correction factor is also proposed which summarises the differences between path lab, finger pricking and measured values using experimental setup.

Chapter 6

Future Scope

The field of non-invasive blood glucose measurement using antennas holds considerable potential for further advancements and improvements. Some areas of future exploration and development include:

1. Miniaturization and Wearable Devices: Efforts can be made to miniaturize the antenna-based devices, making them more portable and comfortable for everyday use. Integration of these devices into wearable technologies, such as smartwatches or patches, can provide individuals with continuous glucose monitoring in a convenient and unobtrusive manner.

2. Enhanced Accuracy and Calibration: Researchers can focus on improving the accuracy of non-invasive glucose measurement techniques by refining calibration algorithms and signal processing methods. Advancements in machine learning and artificial intelligence can be leveraged to enhance the accuracy of predictions and reduce potential errors or interferences.

3. Long-term Reliability and Stability: Ensuring the long-term reliability and stability of non-invasive glucose measurement systems is crucial for their widespread adoption. Ongoing research should address challenges such as sensor drift, signal interference, and environmental factors to ensure consistent and accurate measurements over extended periods.

4. Integration with Digital Health Platforms: Integration of non-invasive glucose measurement devices with digital health platforms can provide users with comprehensive insights into their

diabetes management. By combining glucose data with other health parameters, such as physical activity, heart rate, and sleep patterns, personalized and data-driven recommendations can be generated to optimize diabetes care.

5. Regulatory Approvals and Commercialization: To make non-invasive glucose measurement devices widely available, obtaining regulatory approvals and commercialization are essential. Continued collaboration between researchers, medical professionals, and industry stakeholders is necessary to navigate the regulatory landscape and bring these innovations to the market.

List of Publications

1. Pratik J Mhatre , Dr Manjusha Joshi , " HUMAN BODY MODEL WITH BLOOD FLOW PROPERTIES FOR NON-INVASIVE BLOOD GLUCOSE MEASUREMENT " Biomedical Signal Processing and Control , Elsevier , Nov 2021 [SCIE Journal]

2. Pratik J Mhatre , Dr Manjusha Joshi ," Electrically small Wearable Tunable antenna that fits into smartwatch dial ", IEEE 8th International Conference for Convergence in Technology (I2CT), Pune. Scopus Indexed IEEE conference (H Indexing 7) [Paper Accepted – Will be presented offline 7-9 April 2023]

3. Pratik J Mhatre , Dr Manjusha Joshi ," Design & Verification of non Invasive wearable continuous blood Glucose monitoring system for smart watches ", [Paper Accepted in Progress in Electromagnetic Research Journal- SCIE]

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